

09/288,556

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|--------------|----|--------|--|
| NEWS         | 1  |        | Web Page URLs for STN Seminar Schedule - N. America  |
| NEWS         | 2  |        | "Ask CAS" for self-help around the clock   |
| NEWS         | 3  | SEP 09 | CA/CAPLUS records now contain indexing from 1907 to the present  |
| NEWS         | 4  | DEC 08 | INPADOC: Legal Status data reloaded  |
| NEWS         | 5  | SEP 29 | DISSABS now available on STN   |
| NEWS         | 6  | OCT 10 | PCTFULL: Two new display fields added  |
| NEWS         | 7  | OCT 21 | BIOSIS file reloaded and enhanced  |
| NEWS         | 8  | OCT 28 | BIOSIS file segment of TOXCENTER reloaded and enhanced   |
| NEWS         | 9  | NOV 24 | MSDS-CCOHS file reloaded   |
| NEWS         | 10 | DEC 08 | CABA reloaded with left truncation   |
| NEWS         | 11 | DEC 08 | IMS file names changed   |
| NEWS         | 12 | DEC 09 | Experimental property data collected by CAS now available in REGISTRY  |
| NEWS         | 13 | DEC 09 | STN Entry Date available for display in REGISTRY and CA/CAPLUS   |
| NEWS         | 14 | DEC 17 | DGENE: Two new display fields added  |
| NEWS         | 15 | DEC 18 | BIOTECHNO no longer updated  |
| NEWS         | 16 | DEC 19 | CROPU no longer updated; subscriber discount no longer available   |
| NEWS         | 17 | DEC 22 | Additional INPI reactions and pre-1907 documents added to CAS databases  |
| NEWS         | 18 | DEC 22 | IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields  |
| NEWS         | 19 | DEC 22 | ABI-INFORM now available on STN  |
| NEWS EXPRESS |    |        | DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003 |
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FILE 'HOME' ENTERED AT 18:57:08 ON 07 JAN 2004

09/288,556

=> file reg  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |
| 0.21       | 0.21    |

FILE 'REGISTRY' ENTERED AT 18:57:19 ON 07 JAN 2004  
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STRUCTURE FILE UPDATES: 5 JAN 2004 HIGHEST RN 634558-38-6  
DICTIONARY FILE UPDATES: 5 JAN 2004 HIGHEST RN 634558-38-6

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

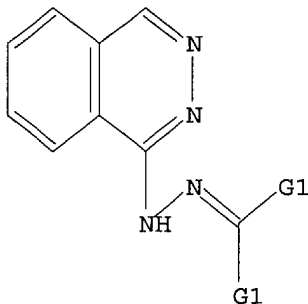
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>  
Uploading 087951.str

L1 STRUCTURE UPLOADED

=> d l1  
L1 HAS NO ANSWERS  
L1 STR



G1 C,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full  
FULL SEARCH INITIATED 18:58:24 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 1979 TO ITERATE

100.0% PROCESSED 1979 ITERATIONS  
SEARCH TIME: 00.00.01

288 ANSWERS

L2 288 SEA SSS FUL L1

09/288,556

=> file caplus  
COST IN U.S. DOLLARS

| SINCE FILE | TOTAL   |
|------------|---------|
| ENTRY      | SESSION |
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FULL ESTIMATED COST

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FILE COVERS 1907 - 7 Jan 2004 VOL 140 ISS 2  
FILE LAST UPDATED: 6 Jan 2004 (20040106/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2 and stabilized  
162 L2  
140641 STABILIZED  
2 STABILIZEDS  
140643 STABILIZED  
(STABILIZED OR STABILIZEDS)  
L3 0 L2 AND STABILIZED

=> s l2 and stability  
162 L2  
566487 STABILITY  
22108 STABILITIES  
577284 STABILITY  
(STABILITY OR STABILITIES)  
L4 7 L2 AND STABILITY

=> d l4 1-7 ibib abs hitstr

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:892084 CAPLUS  
DOCUMENT NUMBER: 139:381497  
TITLE: Preparation of stable hydralazine derivatives  
INVENTOR(S): Barbeau, Donald L.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S.  
Ser. No. 87,951.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

09/288,556

|               |    |          |                |          |
|---------------|----|----------|----------------|----------|
| US 2003212272 | A1 | 20031113 | US 2002-306196 | 20021127 |
| US 2003199512 | A1 | 20031023 | US 2002-87951  | 20020305 |
| WO 2003075928 | A2 | 20030918 | WO 2003-US6521 | 20030304 |
| WO 2003075928 | A3 | 20031204 |                |          |

W: AU, BR, CA, IL, IN, JP, KR, MX, NO, NZ, PH, RU

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.:

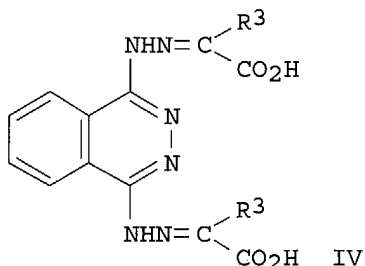
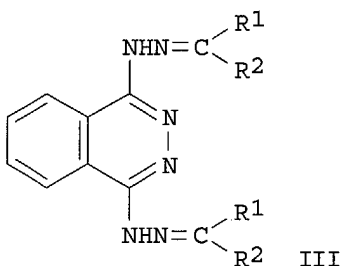
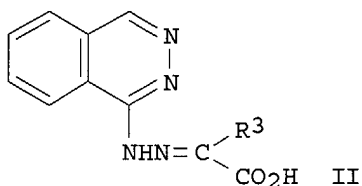
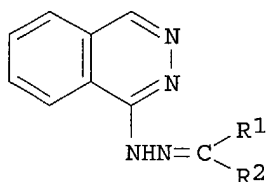
US 2002-87951 A2 20020305

US 2002-306196 A 20021127

OTHER SOURCE(S):

MARPAT 139:381497

GI



AB A method of improving the **stability** of a hydralazine compn. during manufg. or storage comprises coupling an N-protecting group with hydralazine to produce title compds. [I-IV; R1, R2 = H, (substituted) alkyl, aryl, cycloalkyl, aralkyl, alkylcycloalkyl, alkenyl; R1R2 = atoms to form a (substituted) C4-7 cycloalkyl; R3 = alkyl, (substituted) aryl, aralkyl, cycloalkyl, aralkyl, alkylcycloalkyl, (CH2)nCOOH; n = 1-7], were prepd. (no data). Thus, 1-hydrazinophthalazine hydrochloride and .alpha.-ketoglutaric acid were stirred overnight in H2O to give 88% 1-hydrazinophthalazine .alpha.-ketoglutarate hydrazone.

IT 56173-18-3P 61641-43-8P 67173-21-1P

67536-13-4P 77874-88-5P 82928-49-2P

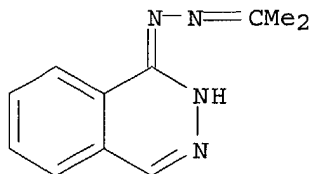
600707-30-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of stable hydralazine derivs.)

RN 56173-18-3 CAPLUS

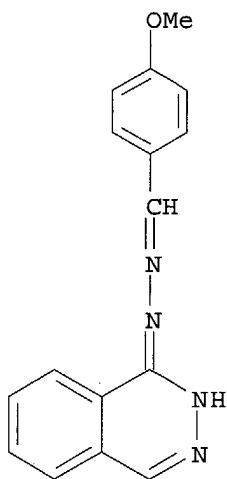
CN 1(2H)-Phthalazinone, (1-methylethylidene)hydrazone (9CI) (CA INDEX NAME)



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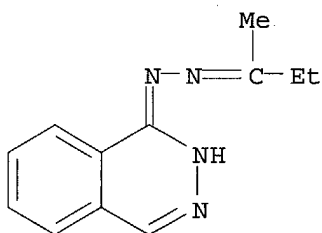
RN 61641-43-8 CAPLUS

CN Benzaldehyde, 4-methoxy-, 1-phthalazinyldiazine (9CI) (CA INDEX NAME)



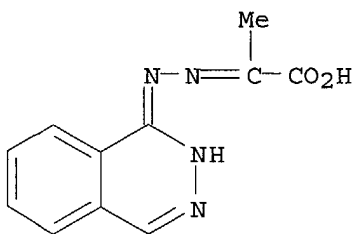
RN 67173-21-1 CAPLUS

CN 2-Butanone, 1-phthalazinyldiazine (9CI) (CA INDEX NAME)



RN 67536-13-4 CAPLUS

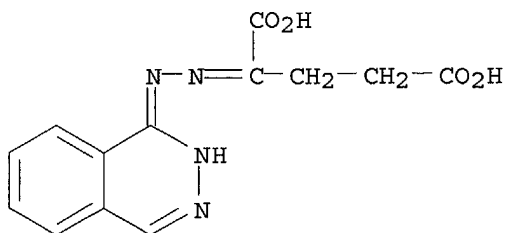
CN Propanoic acid, 2-(1-phthalazinyldiazono)- (9CI) (CA INDEX NAME)



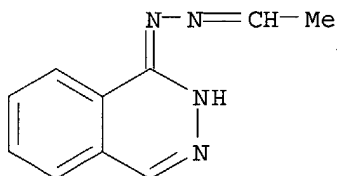
RN 77874-88-5 CAPLUS

CN Pentanedioic acid, 2-(1-phthalazinyldiazono)- (9CI) (CA INDEX NAME)

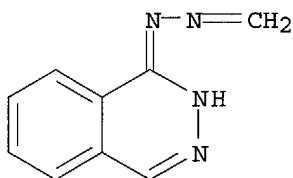
09/288,556



RN 82928-49-2 CAPLUS  
CN Acetaldehyde, 1-phthalazinylhydrazone (9CI) (CA INDEX NAME)



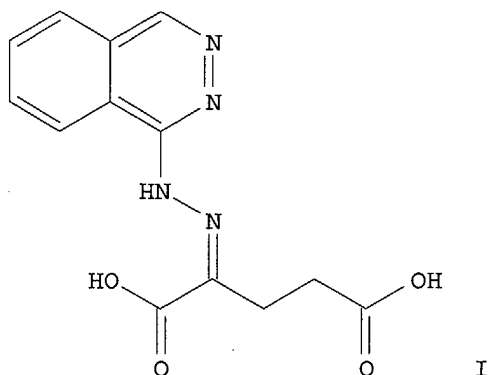
RN 600707-30-0 CAPLUS  
CN 1(2H)-Phthalazinone, methylenehydrazone (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:737585 CAPLUS  
DOCUMENT NUMBER: 139:265755  
TITLE: Stable hydralazine derivative hydrazone pharmaceutical compositions  
INVENTOR(S): Barbeau, Donald L.  
PATENT ASSIGNEE(S): USA  
SOURCE: PCT Int. Appl., 62 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.   | KIND | DATE              | APPLICATION NO. | DATE       |
|--|------|-------------------|-----------------|------------|
| WO 2003075928  | A2   | 20030918          | WO 2003-US6521  | 20030304   |
| WO 2003075928  | A3   | 20031204          |                 |            |
| W: AU, BR, CA, IL, IN, JP, KR, MX, NO, NZ, PH, RU  |      |                   |                 |            |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR |      |                   |                 |            |
| US 2003199512  | A1   | 20031023          | US 2002-87951   | 20020305   |
| US 2003212272  | A1   | 20031113          | US 2002-306196  | 20021127   |
| PRIORITY APPLN. INFO.:   |      |                   | US 2002-87951   | A 20020305 |
|  |      |                   | US 2002-306196  | A 20021127 |
| OTHER SOURCE(S):   |      | MARPAT 139:265755 |                 |            |
| GI   |      |                   |                 |            |

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AB Hydralazine deriv. hydrazones such as I were prepd. for stable pharmaceuticals. I and other derivs. were tested for antihypertensive activity and the **stability** of the derivs. detd. in solns.

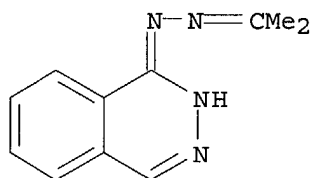
IT 56173-18-3P 61641-43-8P 67173-21-1P  
67536-13-4P 77874-88-5P 82928-49-2P  
600707-30-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(stable hydralazine deriv. hydrazone pharmaceutical compns.)

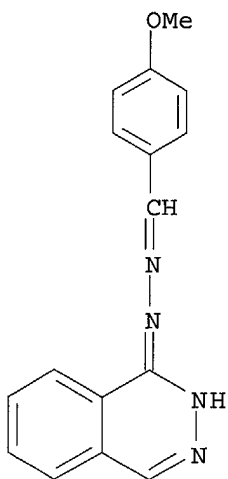
RN 56173-18-3 CAPLUS

CN 1(2H)-Phthalazinone, (1-methylethylidene)hydrazone (9CI) (CA INDEX NAME)



RN 61641-43-8 CAPLUS

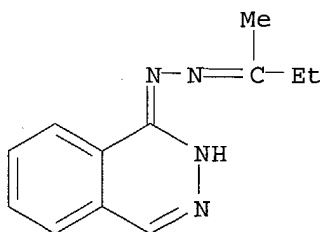
CN Benzaldehyde, 4-methoxy-, 1-phthalazinylhydrazone (9CI) (CA INDEX NAME)



09/288,556

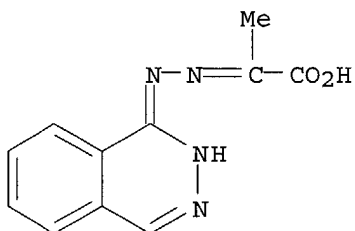
RN 67173-21-1 CAPLUS

CN 2-Butanone, 1-phthalazinyldiazone (9CI) (CA INDEX NAME)



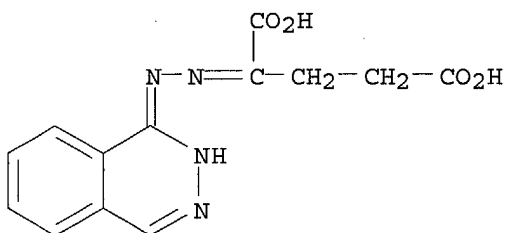
RN 67536-13-4 CAPLUS

CN Propanoic acid, 2-(1-phthalazinyldiazono)- (9CI) (CA INDEX NAME)



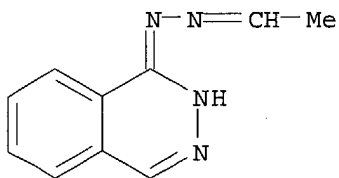
RN 77874-88-5 CAPLUS

CN Pentanedioic acid, 2-(1-phthalazinyldiazono)- (9CI) (CA INDEX NAME)



RN 82928-49-2 CAPLUS

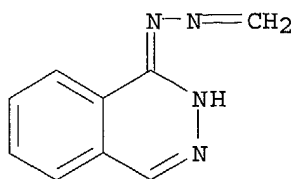
CN Acetaldehyde, 1-phthalazinyldiazone (9CI) (CA INDEX NAME)



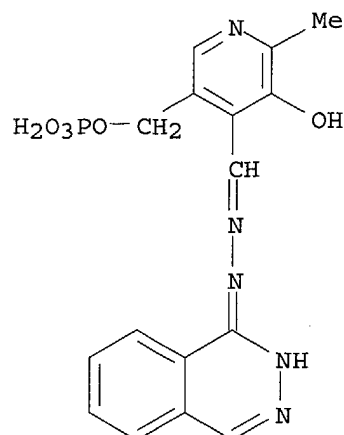
RN 600707-30-0 CAPLUS

CN 1(2H)-Phthalazinone, methylenediazone (9CI) (CA INDEX NAME)





L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1998:355491 CAPLUS  
 DOCUMENT NUMBER: 129:130899  
 TITLE: Kinetic study of the reaction of pyridoxal 5'-phosphate with hydrazino compounds of pharmacological activity  
 AUTHOR(S): Echevarria-Gorostidi, Gerardo R.; Basagoitia, Andrea; Pizarro, Eliana; Goldsmid, Ruth; Santos Blanco, Jose G.; Garcia Blanco, Francisco  
 CORPORATE SOURCE: Department Physical Chemistry, University Alcala, Alcala de Henares, E-28871, Spain  
 SOURCE: Helvetica Chimica Acta (1998), 81(5), 837-844  
 CODEN: HCACAV; ISSN: 0018-019X  
 PUBLISHER: Verlag Helvetica Chimica Acta AG  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The kinetics of the reaction between pyridoxal 5'-phosphate (PLP) with carbidopa, hydralazine, and isoniazid, in aq. soln. at variable pH and const. ionic strength of 0.1M was studied spectrophotometrically. The rate consts. of formation and hydrolysis of the resulting Schiff base, and its **stability** were detd. in a wide range of pH. A comparison is made of the formation rate consts. with those of PLP with hydrazine. The reactivity shows the sequence isoniazid > hydrazine > carbidopa > hydralazine in the whole range of pH studied. The Schiff bases studied are more stable than those formed by PLP and hexylamine and as stable as those described for the reactions of PLP with poly(L-lysine) or copolypeptides contg. L-lysine.  
 IT 13284-03-2  
 RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
 (kinetics of the reaction of pyridoxal 5'-phosphate with hydrazino compds. of pharmacol. activity)  
 RN 13284-03-2 CAPLUS  
 CN 4-Pyridinecarboxaldehyde, 3-hydroxy-2-methyl-5-[(phosphonoxy)methyl]-, 1-phthalazinylhydrazone (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:491992 CAPLUS

DOCUMENT NUMBER: 121:91992

TITLE: Spectrophotometric and chromatographic (HPLC) analysis of hydralazine, dihydralazine and hydrazine after derivatization with 2-nitrocinnamaldehyde

AUTHOR(S): Di Pietra, Anna Maria; Roveri, Paola; Gotti, Roberto; Cavrini, Vanni

CORPORATE SOURCE: Dip. Sci. Farm., Univ. Bologna, Bologna, 40126, Italy

SOURCE: Farmaco (1993), 48(11), 1555-67

CODEN: FRMCE8; ISSN: 0014-827X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A simple spectrophotometric method, based on the reaction with 2-nitrocinnamaldehyde, was developed for the detn. of hydralazine ( $\lambda_{\text{max}}$  = 390 nm) and dihydralazine ( $\lambda_{\text{max}}$  = 395 nm) in their dosage forms. The method was **stability**-indicating and showed results comparable to those obtained by a ref. HPLC (cyano column) method. Prechromatog. derivatization with 2-nitrocinnamaldehyde, in combination with a preliminary solid-phase extn. (C18 sorbent), enabled sensitive and selective HPLC detns. of hydrazine in hydralazine to be accomplished.

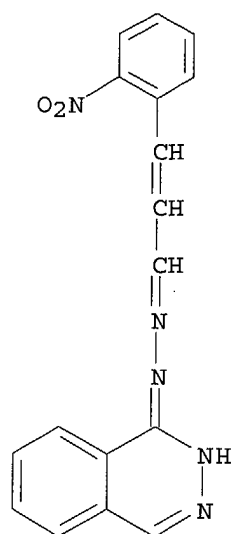
IT 156568-79-5P

RL: PREP (Preparation)

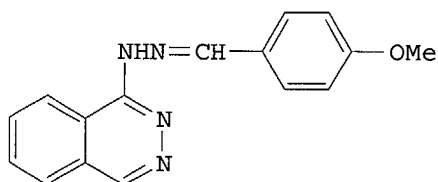
(prepn. of, in drug detn. by spectrophotometry)

RN 156568-79-5 CAPLUS

CN 2-Propenal, 3-(2-nitrophenyl)-, 1-phthalazinylhydrazone (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1989:417044 CAPLUS  
 DOCUMENT NUMBER: 111:17044  
 TITLE: **Stability** problems with hydralazine  
 p-anisaldehyde hydrazone  
 AUTHOR(S): Semple, Hugh A.; Tam, Yun K.; Croteau, Stephen M.;  
 Coutts, Ronald T.  
 CORPORATE SOURCE: Fac. Pharm. Pharm. Sci., Univ. Alberta, Edmonton, AB,  
 T6G 2N8, Can.  
 SOURCE: Journal of Pharmaceutical Sciences (1989), 78(5),  
 432-4  
 CODEN: JPMSAE; ISSN: 0022-3549  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



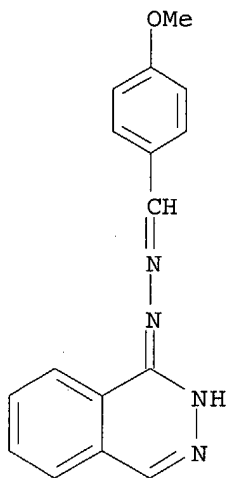
I

- AB Hydralazine was detd. in blood by HPLC with UV detection based on derivatization with p-anisaldehyde and formation of I. However, I and its 4-methyl hydralazine analog, used as the internal std., were unstable in fresh canine blood contg. EDTA as an anticoagulant, human citrated blood, and fresh human blood contg. EDTA. The instability may lead to sample decompn. and hence variability and possible errors in detn. of hydralazine concn. p-Nitrobenzaldehyde produced a more stable deriv. with otherwise similar characteristics to I. Thus, p-nitrobenzaldehyde was recommended as a derivatizing agent in hydralazine HPLC detn. in blood.
- IT **61641-43-8**, Hydralazine p-anisaldehyde hydrazone  
 RL: PRP (Properties)  
 (**stability** of, in blood of human and lab. animals,  
 hydralazine HPLC detn. in relation to)

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RN 61641-43-8 CAPLUS

CN Benzaldehyde, 4-methoxy-, 1-phthalazinylhydrazone (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:485608 CAPLUS

DOCUMENT NUMBER: 109:85608

TITLE: Assay for hydralazine as its stable  
p-nitrobenzaldehyde hydrazone

AUTHOR(S): Semple, Hugh A.; Tam, Yun K.; Tin, Sarah; Coutts,  
Ronald T.

CORPORATE SOURCE: Fac. Pharm. Pharm. Sci., Univ. Alberta, Edmonton, AB,  
T6G 2N8, Can.

SOURCE: Pharmaceutical Research (1988), 5(6), 383-6

CODEN: PHREEB; ISSN: 0724-8741

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new method for the detn. of the antihypertensive drug, hydralazine, in human and dog blood is described that involves the addn. of p-nitrobenzaldehyde to blood samples contg. hydralazine, to form a stable Schiff's base, hydralazine p-nitrobenzaldehyde hydrazone. The deriv. is extd. from the blood into hexane and the samples are dried under a N stream. The exts. are then dissolved in mobile phase and analyzed by HPLC. The extd. samples can be stored for at least 7 days at room temp. or at -20.degree.. The sensitivity of the assay is better than 300 pg/mL using 3-mL blood samples, and the range can extend to 640 ng/mL. The **stability** of the extd. samples plus the sensitivity and simplicity of the assay are the main advantages of the method over other selective methods for hydralazine.

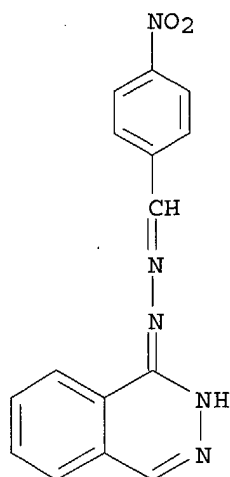
IT 97142-39-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

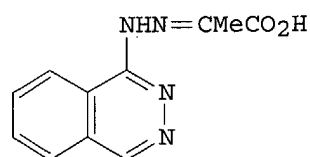
(prepn. of, in hydralazine detn. in blood of humans and lab. animals  
as, by HPLC)

RN 97142-39-7 CAPLUS

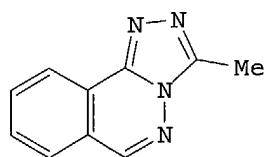
CN Benzaldehyde, 4-nitro-, 1-phthalazinylhydrazone (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1981:52783 CAPLUS  
 DOCUMENT NUMBER: 94:52783  
 TITLE: **Stability** of hydralazine pyruvate hydrazone  
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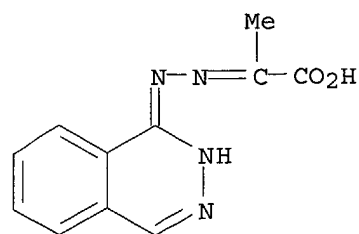


I



II

AB Under acidic conditions in vitro, hydralazine pyruvate hydrazone (I) [67536-13-4] decarboxylated to methyltriazolophthalazine (II) [20062-41-3], but at physiol. pH little breakdown occurred. In vivo, I was metabolized to CO<sub>2</sub>, as shown by expts. with rats.  
 IT 67536-13-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (decarboxylation of, to methyltriazolophthalazine)  
 RN 67536-13-4 CAPLUS  
 CN Propanoic acid, 2-(1-phthalazinylhydrazono)- (9CI) (CA INDEX NAME)



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